Figure 1a: Synthesis of 3'-valinyl esters of 2'-deoxy- β -L-cytidine

Figure 1b: Synthesis of 5'-valinyl esters of 2'-deoxy-β-L-cytidine

Figure 2: Synthesis of N^4 -acetyl-2'-deoxy- β -L-cytidine

Figure 3: Synthesis of N^4 -[(dimethylamino)methylene]-2'-deoxy- β -L-cytidine

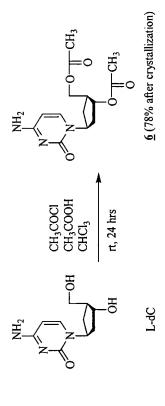


Figure 4: Synthesis of 3',5'-di-O-acetyl-2'-deoxy-β-L-cytidine

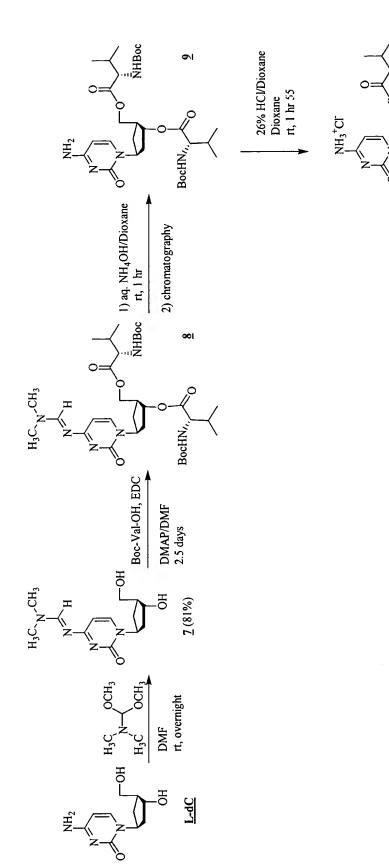


Figure 5: Synthesis of 3',5'-di-O-valinyl esters of 2'-deoxy β-L-cytidine

<u>10</u>(overall yield 45%)

Figure 6: Synthesis of N^4 -Boc-valinyl ester of 2'-deoxy- β -L-cytidine

Figure 7: Synthesis of 3',5', N⁴-tri-(L-valinyl)-L-2'-deoxycytidine

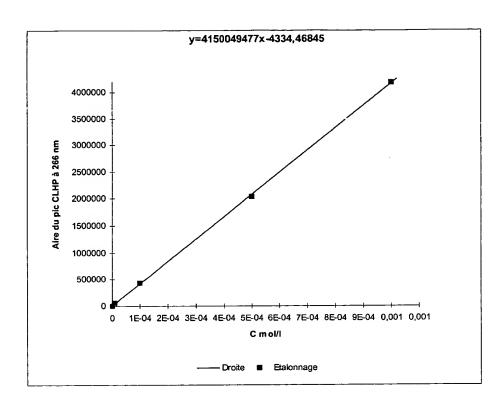


Figure 8a: Solubility Calibration Curve for D-dC

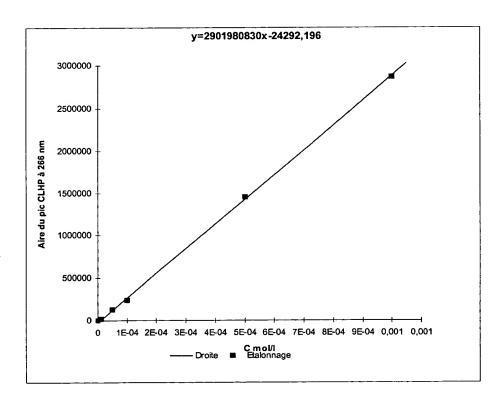


Figure 8b: Solubility Calibration Curve for the 3',5'-Divalinyl Ester of L-dC

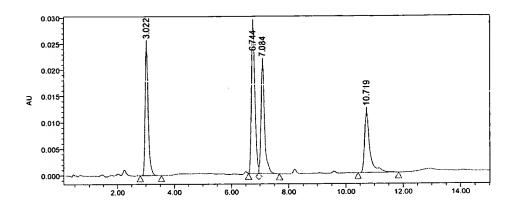


Figure 9a: HPLC profile – 7.5 hours at pH of 7.42

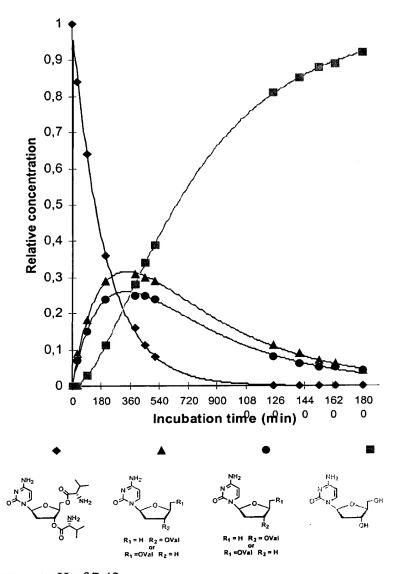


Figure 9b: Kinetics curves at pH of 7.42

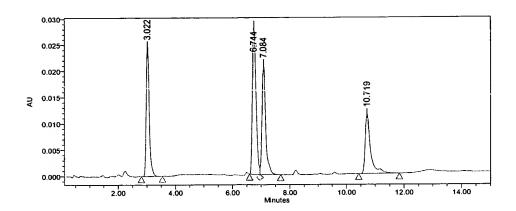


Figure 10a: HPLC profile – 5.33 hours at pH of 7.20

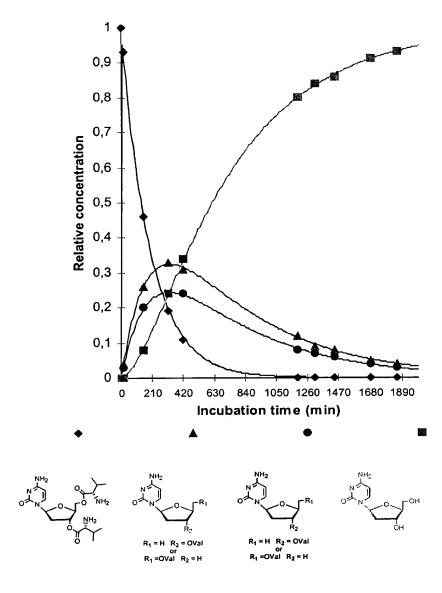


Figure 10b: Kinetics curves at pH of 7.20

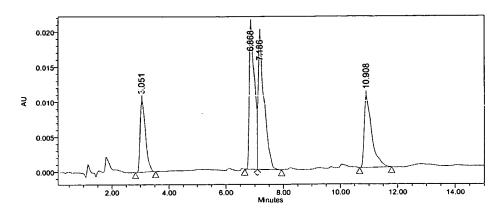


Figure 11a: HPLC profile – 95.7 hours at pH of 4.51

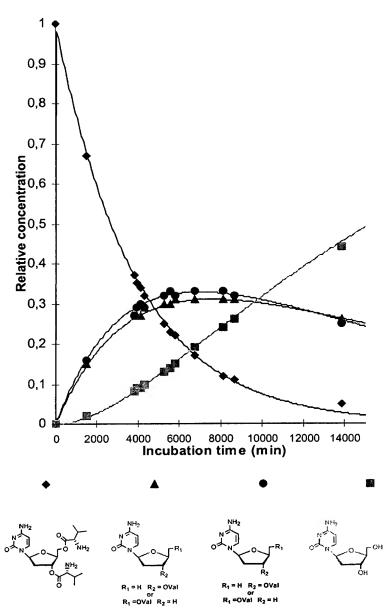


Figure 11b: Kinetics curves at pH of 4.51

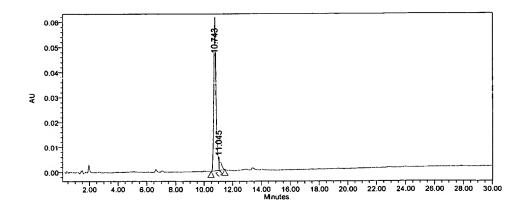


Figure 12: HPLC profile – 48 hours at pH of 1.23

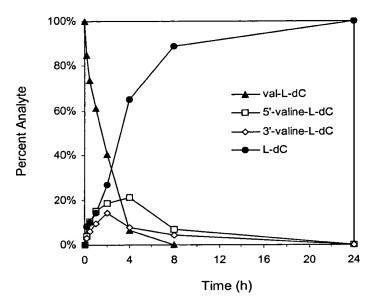


Figure 13 In Vitro Metabolism of 3',5'-Dival-L-dC in Human Plasma

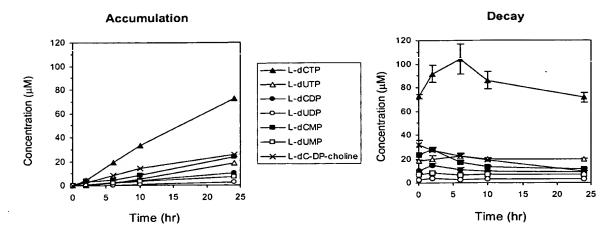


Figure 14 Intracellular Metabolism of L-dC in HepG2 Cells

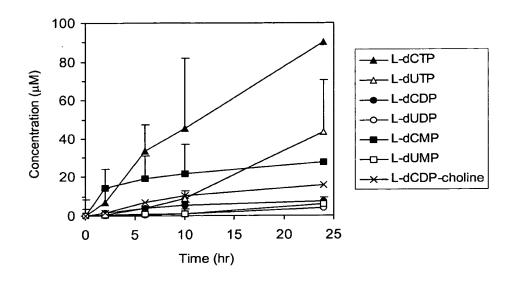


Figure 15 Intracellular Metabolism of L-dC in Primary Human Hepatocytes

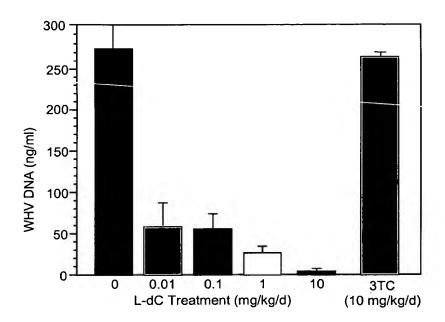


Figure 16 Antiviral Dose Response of L-dC in the Woodchuck Model

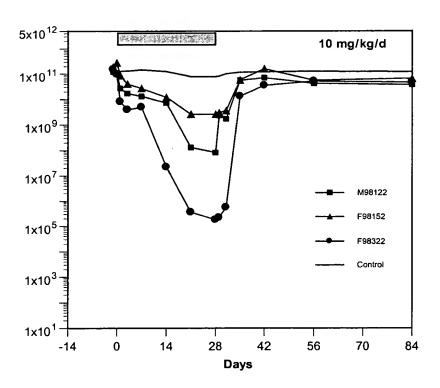


Figure 17 Antiviral Activity of L-dC in the Woodchuck Model

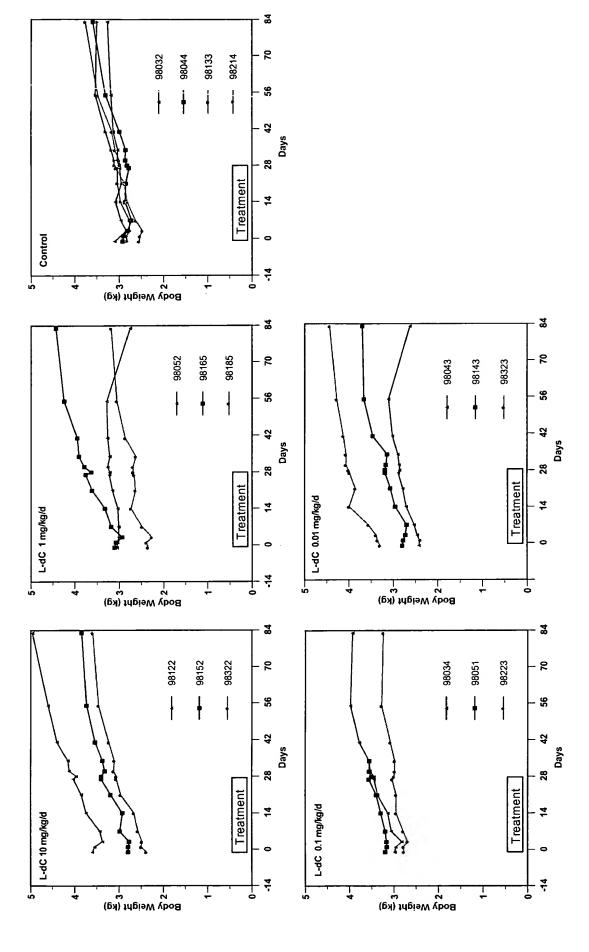


Figure 18 Body Weights of Woodchucks Orally Treated with L-dC - 28 Days

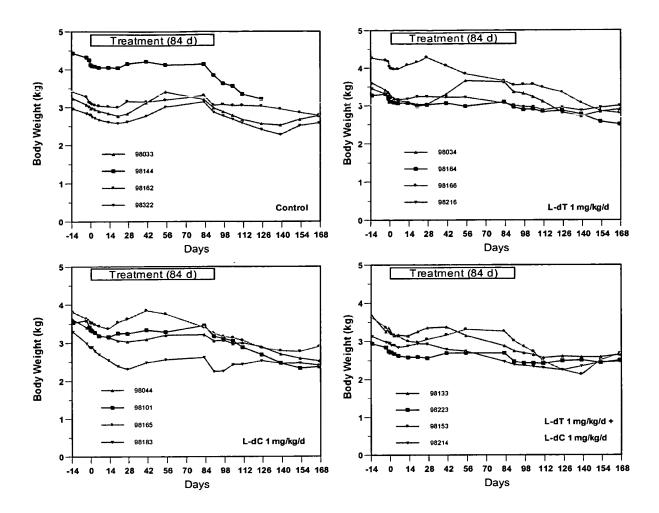


Figure 19 Body Weights of Woodchucks Orally Treated with L-dC – 12 Weeks